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Acute Effect of Passive Smoking on Lung Function and Airway Responsiveness in Asthmatic Children

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Summary. The effect of a 1-hour exposure at rest during passive cigarette smoking (20 ppm CO) or Sham was investigated in 11 children with bronchial asthma (age range, 8–13 yr; ten boys, one girl). Nine of the subjects were on regular therapy with inhaled β_2-agonists and disodium cromoglycate. Both drugs were withheld at least 6 hours prior to each study session. Exposure was performed in an environmental chamber. Before and immediately after exposure, lung function and symptom scores were determined. After exposure, a histamine inhalation challenge was performed to determine the concentrations that caused a 100% increase in SRaw (PC_{100}SRaw) and a 20% fall in FEV_1, ($PC_{20}FEV_1$). Mean (SD) SRaw before and after Sham was 8.7 (3.6) and 9.0 (3.2) cmH_2O·s, and mean FEV_1 (SD) was 1.97 (0.32) and 1.98 (0.40) L, respectively. Before and after cigarette smoking, mean SRaw (SD) was 10.4 (5.3) and 9.4 (3.3) cmH_2O·s, and mean FEV_1 (SD) was 1.95 (0.37) and 1.94 (0.35 L, respectively. Geometric mean (SD) PC_{100}SRaw and $PC_{20}FEV_1$ after Sham was 1.39 (3.0) and 0.70 (2.7) mg/mL, and after passive smoking 1.65 (2.5) and 0.96 (2.3) mg/mL, respectively. There were no statistical differences in lung function and PC values between Sham and passive cigarette smoking. The main symptoms during passive smoking were irritation of the eye and the nasopharynx. Our observations suggest that in children with mild bronchial asthma 1 hour of passive cigarette smoking does not cause consistent changes of lung function and bronchial responsiveness. Pediatr Pulmonol 1991; 10:123–131.

Key words: Environmental chamber exposure; pre-exposure and Sham exposure comparisons; symptom scores; specific airway resistance and FEV_1; $PC_{histamine}$; urinary cotinine concentration

INTRODUCTION

Subjects with bronchial asthma are characterized by airway hyperresponsiveness to a variety of stimuli. Cigarette smoke is considered to be a common stimulus that may affect subjects with asthma.[1–3] In children, the adverse effect of chronic passive smoking on respiratory symptoms has received increasing attention.[4–7] In some of these investigations an association between parental smoking habits and acute lower respiratory illness,[8–12] respiratory symptoms,[13–16] prevalence and severity of asthma,[13,17,18] impaired lung function, and bronchial responsiveness[10,12,13,16,17,19–23] could be demonstrated. In contrast to chronic exposure, little is known on the acute effect of passive smoking in children. We therefore studied symptoms, lung function, and airway responsiveness of children with bronchial asthma before and after 1 hour exposure to cigarette smoke as compared to control conditions.

MATERIALS AND METHODS

Patients

We investigated 11 children (10 boys, 1 girl) with allergic bronchial asthma ranging in age from 8 to 13 years [mean (SD) 10.4 (1.4) yr]. Individual patient characteristics are given in Table 1.

The diagnosis of bronchial asthma was established in all children within at least 1 year before entering the study and patients had been followed for a longer period of time in our out-patient department. The children were not selected on symptoms induced by previous exposure to cigarette smoke. Diagnosis was based on typical symptoms, reversible airflow obstruction, bronchial hyperresponsiveness to histamine, and a positive prick skin test to at least one common allergen (Allergopharma, Reinbek, Germany). Six of 11 patients showed elevated IgE (>150 IE/mL), and 6 children had an

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TABLE 1—Data of Individual Patients

Patient	Sex	Age (yr)	Weight (kg)	Height (cm)	Atopy	IgE (IE/mL)	Eosinophils (counts/mm³)	PEF_{min} (L/min)	PEF_{max} (L/min)	VC[a] L_{BTPS}	FEV_1 (% pred.)	$PC_{20}FEV_1$[b] (mg/mL)	Therapy[c]
1	M	12	50	165	+	92	563	400	480	3.68	97	0.09	B,D
2	M	13	42	154	+	114	350	280	330	2.18	76	0.34	B,D
3	M	11	35	142	+	524	422	320	440	2.35	97	0.73	B,D
4	M	9	38	140	+	219	100	300	380	2.46	110	1.25	B,D
5	M	10	35	150	+	518	441	280	340	2.48	88	1.72	B,D
6	M	11	40	149	+	146	319	300	380	2.60	111	1.02	B,D,iC
7	M	11	41	151	+	101	181	330	400	2.60	107	1.13	B,D
8	M	9	40	141	+	269	143	240	270	1.90	85	0.12	B,D
9	M	8	26	137	+	137	147	210	330	1.82	90	1.28	—
10	M	10	36	142	+	361	422	280	350	3.00	130	0.46	B,D
11	F	10	35	143	+	185	293	150	220	2.20	98	0.30	—
Mean		10.4	38	147		242	307	281	356	2.48	99	0.54	
SD		1.4	6	8		159	149	65	73	0.52	15	2.70	

[a]VC, inspired vital capacity. For other definitions see text.
[b]Geometric mean values and geometric standard deviations of mean.
[c]Therapy: B, inhaled β_2-agonists; D, disodium cromoglycate; iC, inhaled corticosteroids.

increase of eosinophils in peripheral blood (> 300/mm³).

In all subjects the severity of asthma required a long-term therapy, which had to be continued in 9 of 11 children during the study period. All children on therapy received disodium cromoglycate, two puffs two to four times per day. Each puff of disodium cromoglycate (1 mg) was combined with 0.05 mg fenoterol (Ditec) or 0.5 mg reproterol (Aarane) as a β_2-adrenoceptor-agonist. An additional subject inhaled beclomethasone dipropionate (400 µg/day). In all children, this therapeutic regime was sufficient to control the disease and allow normal activities. This is also reflected by the minimum morning, before therapy (PEF_{min}) and maximum daytime peak expiratory flow values (PEF_{max}), which were measured regularly (Table 1). In the 9 asthmatic children receiving regular therapy, the severity of the disease allowed discontinuation of inhalation therapy at least 6 hours prior to each study session without precipitating symptoms or deteriorating lung function (subject no. 6 continued beclomethasone inhalation during the study period).

Spirometry, measured at least 6 hours after inhaling a bronchodilator, was within normal limits. In all children the provocative concentration of inhaled histamine necessary to decrease FEV_1 by 20% from baseline was less than 8 mg/mL (Table 1), thus demonstrating airway hyperresponsiveness (see Histamine Inhalation Challenge, below). During the study period and within the 2 weeks preceding the study no child suffered from an upper respiratory tract infection or experienced an uncommon burden of allergen; therefore, all included children were considered to be currently clinically stable. None of the children had ever actively smoked cigarettes; six of them were exposed to cigarette smoke at home (Table 2). Children and parents were informed about the aim of the study and gave their consent.

Cigarette Smoke Exposure

Exposure Chamber

The study was performed in a 24 m³ exposure chamber. To ensure homogeneous concentration of cigarette smoke the air was moved by fans. Sampling ports were distributed within the chamber to check for gradients of gas concentrations and particle density. Cigarette smoke was generated by a smoking machine designed in our laboratory that took one puff per cigarette per minute (according to DIN 10240). To achieve the target concentration of about 20 ppm CO, on average two cigarettes were smoked simultaneously. We used filter cigarettes of a leading brand with a nicotine content of 0.9 mg and tar content of 13 mg per cigarette.

Measurement of Exposure Conditions

The level of cigarette smoke exposure was determined by measuring CO, NO_x, particle density, nicotine, acetaldehyde, formaldehyde, acrolein, and ammonia. Concentration of CO was measured continously by an infrared gas analyzer (Unor 6N, Maihak AG, Hamburg, Germany); its calibration was checked daily by a certified span gas (Linde AG, Unterschleisshein, Germany). Concentration of NO_x was measured by a chemiluminescence nitrogen oxides analyzer (8840, Monitor Labs Inc., San Diego, CA), which was calibrated regularly by a permeation tube calibrator (model 8550, Monitor Labs Inc., San Diego, CA). Particle density was monitored continuously by measuring optical particle density (RAM-1, GCA/Environmental Instruments, Bedford, MA) using a 4 µm precollector. Optical particle density

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TABLE 2—Ratios of Urinary Cotinine to Creatinine and Reported Parental Smoking Habits

Patients no.	Cotinine/creatinine (ng/mg)	Paternal smoking	Maternal smoking
1	9.4	+	−
2	5.1	+	−
3	33.6	−	−
4	2.8	+	−
5	1.5	−	−
6	0.4	−	+
7	3.5	−	+
8	0	−	−
9	12.5	+	−
10	0	−	−
11	0	−	−

was calibrated in regular intervals gravimetrically by taking filter probes (Millipore, FALP 03700, Type FA) from total sampling volumes of 17–73 litres of air. Nicotine, acetaldehyde, formaldehyde, acrolein, and ammonia were determined using commercially available sample tubes and filters at sampling volumes ranging between 3 and 100 L of air. Analysis was performed by gas chromatography (nicotine), by high performance liquid chromatography (acetaldehyde, formaldehyde, acrolein), and by the indophenol method VDI 2461 (ammonia). Temperature and relative humidity were measured at the beginning and at the end of each exposure.

Estimation of Chronic Smoke Exposure

To estimate chronic passive smoke exposure at home we measured urinary cotinine concentration as a biological marker. Cotinine was determined in triplicate from morning urine specimens collected on the second study day. Urine cotinines were obtained in an environment free of smoking. Urine was stored at −20°C until assayed. Cotinine was measured by RIA[24] and corrected for creatinine excretion (Table 2).

Assessment of Symptoms

The chest of each subject was auscultated before and immediately after exposure. To estimate severity of symptoms induced by exposure, the children and their parents were instructed to check an ordinal scale ranging from 0 to 10 in order to determine severity of eye, nose, and throat irritation, cough, chest tightness, and headache. Zero indicated no perceptible symptom and 10 almost intolerable severity of the respective symptom.

Lung Function Measurement

Airway resistance (Raw) during breathing at 1 Hz frequency and thoracic gas volume (TGV) were measured by a volume-constant body plethysmograph (Bodytest, E. Jaeger, Würzburg, Germany) connected to a Computer (PDP 11/04, Digital Equipment Corp., Maynard, MA). Raw was multiplied by the corresponding TGV to obtain specific airway resistance (SRaw). Raw was measured during up to four breathing cycles. FEV_1 was assessed by a pneumotachograph immediately after body plethysmography. Measurements were repeated four times. For analysis, the average of four values of SRaw and the average of the two maximum values of FEV_1 were computed.

Histamine Inhalation Challenge

Bronchial challenge with histamine was performed according to the guidelines of Chai et al.[25] using a breath-synchronized pressure valve. The aerosols were generated during 0.6 s at the beginning of five slow inspirations from FRC to TLC, the nebulizer output being 80 μL of solution per five nebulizations. Saline solutions of histamine diphosphate (Sigma Chemie, Deisenhofen, Germany) were prepared daily. After a buffer solution, the subjects inhaled doubling concentrations of histamine, starting with 0.05 mg/mL histamine. Lung function was measured 1 and 3 min after inhalation. The challenge was stopped after at least a 100% increase of SRaw and a 20% fall in FEV_1. Dose-response curves were constructed by plotting SRaw and FEV_1 against log histamine concentration. By linear interpolation, the provocative concentrations of histamine (in mg/mL) were computed necessary to increase SRaw by 100% (PC_{100}SRaw) and to decrease FEV_1 by 20% ($PC_{20}FEV_1$) from baseline. With this method, hyperresponsiveness was assumed if PC values were below 8 mg/mL.[26]

Experimental Protocol

Each patient was studied on 3 days within a 2 week period. All investigations were performed at least 6 hours after the last inhalation therapy. On the first day recent history was taken and a physical examination performed. Lung function and airway responsiveness to inhaled histamine were measured. In case of stable clinical conditions, normal lung function, and airway hyperresponsiveness, the children and their parents were instructed about the experimental procedure. They were provided with sampling probes for collecting morning urinary specimens. Exposures to ambient air (Sham) and to cigarette smoke were performed on the second and third study days, respectively.

On exposure days, subjects rested for 10 min after entering the laboratory. After auscultation of the chest, assessment of symptoms, and measurement of baseline lung function, the children entered the exposure chamber. They were always seated at the same place inside the chamber. Five minutes before the end of exposure, symptoms were assessed again. Immediately after exposure, auscultation of the chest and lung function mea-

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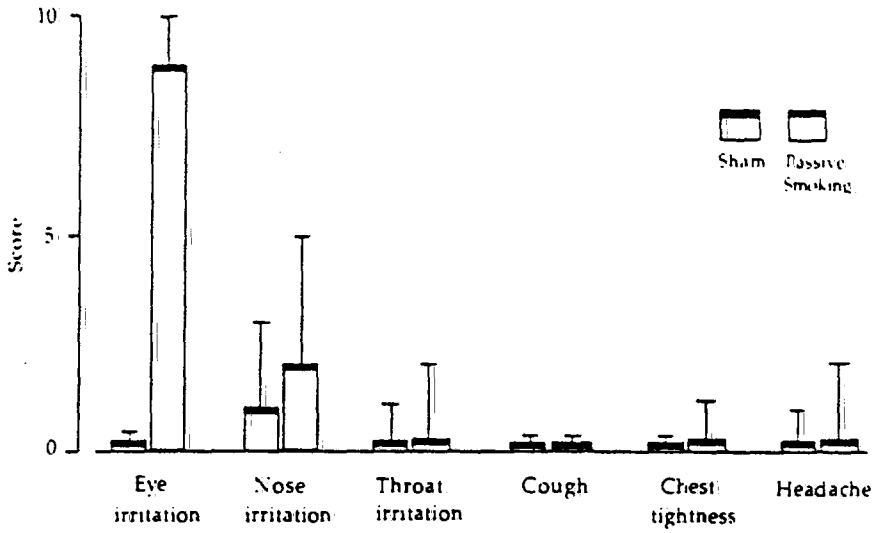

Fig. 1. Median and 90% percentile of symptom score after Sham and passive smoke exposure.

surement were performed. Histamine inhalation challenge was started 15 min after the end of exposure.

Statistical Analysis

The hypothesis of normal distribution of data was tested by normal probability plots and tests. We performed a two-way ANOVA (random factor patient) on the lung function data of the control day and before and after Sham or exposure to smoking. Lung function data before and after Sham or exposure were analyzed by pooling all patients and by a two-way ANOVA. This analysis should reveal a specific effect of exposure by testing the interaction term. We have chosen paired t-tests as a posteriori tests after applying the appropriate Bonferroni correction of the multiplicity of tests.[27] Lung function parameters before and after both exposures and control values were compared by the paired t-test. We performed paired t-tests also on the differences between before-after and during exposure to Sham or ETS, therefore adjusting for possible differences in baseline values between exposure days. PC values were analyzed as logarithms as is common in the literature, and the log PC values after both exposures and the control values were also compared by paired t-tests. Statistical significance was assumed for $P < 0.05$.

RESULTS

Exposure Conditions

During Sham and cigarette smoke exposure, mean (SD) environmental temperature was 24.1 (1.6)°C and mean relative humidity was 51 (3)%, with no difference between the study days. During passive smoke exposure, mean (SD) total particle density was 2,743 (348) $\mu g/m^3$ and nicotine content was 397 (78) $\mu g/m^3$. Mean (SD) concentrations were 20.5 (0.5) ppm for CO, 0.90 (0.09) ppm for NO_x, 0.13 (0.01) ppm for formaldehyde; 0.50 (0.05) ppm for acetaldehyde, 0.081 (0.017) ppm for acrolein, and 5.69 (3.35) ppm for ammonia. During exposure with ambient air, mean (SD) CO was 0.1 (0.3) ppm and mean (SD) total particle density was 17 (57) $\mu g/m^3$.

Symptoms During Exposure

In all children, auscultation of the chest revealed normal breath sounds before and after exposure to Sham and cigarette smoke, respectively. Eye irritation was experienced by all subjects during smoke exposure (Fig. 1). Nasal congestion was reported by 9/11 children after cigarette exposure and 5/11 after Sham. After smoke exposure, throat irritation occured in 3/11, cough in 0/11, chest tightness in 3/11, and headache in 3/11 children. Except for eye irritation, the frequency and intensity of the symptoms did not differ between cigarette smoke and Sham exposure (Fig. 1).

Variability of Baseline Lung Function

Mean (SD) SRaw before Sham and smoke exposure was 8.7 (3.6) and 10.4 (5.3) $cmH_2O \cdot s$, respectively. These values were not significantly different from each other nor from the mean (SD) SRaw value of 8.5 (2.8) $cmH_2O \cdot s$ measured upon entry into the study (control; Table 3). Mean (SD) FEV_1 before Sham and cigarette smoke was 1.97 (0.32) and 1.95 (0.39) L, respectively. These values were not significantly different from each other nor from the mean (SD) FEV_1 value of 1.95 (0.39) L when entering the study (control; Table 3). Mean (SD) values of individual coefficients of variation for the three

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TABLE 3—SRaw (in $cmH_2O \cdot s$) and FEV_1 (in L) Before (Pre) and After (Post) Exposure to Ambient Air (Sham) or Passive Smoking and at the Control Day

	Control		Sham				Passive smoking			
			SRaw		FEV_1		SRaw		FEV_1	
Patient	SRaw	FEV_1	Pre	Post	Pre	Post	Pre	Post	Pre	Post
1	13.2	2.68	12.5	10.6	2.60	2.84	9.9	11.1	2.76	2.81
2	8.1	1.74	5.9	7.9	1.93	1.86	8.6	9.4	1.84	1.82
3	10.7	1.75	12.6	12.8	1.75	1.57	9.6	8.8	1.74	1.97
4	10.1	1.90	4.6	7.3	2.13	2.11	11.1	9.3	1.83	1.84
5	10.5	1.86	11.9	12.7	1.71	1.75	14.3	14.0	1.47	1.55
6	8.1	2.30	9.0	7.8	2.27	2.32	10.5	8.8	2.23	2.26
7	5.2	2.28	5.8	4.2	2.21	2.33	4.6	4.4	2	1.74
8	4.0	1.52	6.6	7.2	1.76	1.75	6.4	6.2		1.78
9	5.4	1.47	3.5	4.4	1.82	1.69	5.5	5.4	1.29	1.72
10	10.8	2.33	13.9	13.0	2.07	2.10	23.9	15.0	2.21	2.13
11	7.8	1.64	9.7	10.6	1.47	1.50	9.7	10.6	1.63	1.71
Mean	8.5	1.95	8.7	9.0	1.97	1.98	10.4	9.4	1.95	1.94
SD	2.8	0.39	3.6	3.2	0.32	0.40	5.3	3.3	0.39	0.35

repeated determinations of SRaw and FEV_1 were 21 (11) and 6 (4)%, respectively.

Lung Function Changes During Exposure

Mean (SD) SRaw before and after 1 hour exposure to ambient air (Sham) was 8.7 (3.6) and 9.0 (3.2) $cmH_2O \cdot s$ with no statistically significant difference (Table 3). Mean (SD) FEV_1 before and after Sham was 1.97 (0.32) and 1.98 (0.40) L with no significant difference. The mean (SD) change of SRaw was 0.23 (1.48) $cmH_2O \cdot s$, and the mean (SD) change of FEV_1 was 0.01 (0.11) L. In percentages the changes of SRaw and FEV_1 induced by Sham ranged from −28 to +59% and from −10 to +9%, respectively.

Mean (SD) SRaw before and after 1 hour exposure to cigarette smoke was 10.4 (5.3) and 9.4 (3.3) $cmH_2O \cdot s$. Mean (SD) FEV_1 before and after smoke exposure was 1.95 (0.39) and 1.94 (0.35) L (Table 3, Fig. 2). Values before and after exposure were not significantly different. The mean (SD) change of SRaw was −1.01 (2.79) $cmH_2O \cdot s$, and the mean (SD) change of FEV_1 was −0.01 (0.21) L. In percentages the changes of SRaw and FEV_1 during passive smoking ranged from −37 to +12% and from −25 to +13%, respectively.

Airway Responsiveness During Exposure

Geometric mean (SD) $PC_{100}SRaw$ and $PC_{20}FEV_1$ before entry (control) were 0.85 (2.4) and 0.54 (2.7) mg/mL (Table 4). Geometric mean (SD) $PC_{100}SRaw$ and $PC_{20}FEV_1$ measured after Sham were 1.39 (3.0) and 0.70 (2.7) mg/mL. Geometric mean (SD) $PC_{100}SRaw$ and $PC_{20}FEV_1$ after exposure to cigarette smoke were 1.65 (2.5) and 0.96 (2.3) mg/mL (Table 4). $PC_{100}SRaw$ and $PC_{20}FEV_1$ were not significantly different between Sham, cigarette smoke exposure and control. As determined from Sham and control, the mean (SD) values of individual variability of $PC_{100}SRaw$ and $PC_{20}FEV_1$ were 1.0 (0.5) and 0.9 (0.6) doubling concentrations of histamine.

DISCUSSION

Our observations demonstrate that in children with mild bronchial asthma 1 hour of passive smoking produced mainly eye irritation but no consistent changes of lung function and bronchial responsiveness to inhaled histamine. Acute pulmonary response to passive smoking has not been studied in asthmatic children. Previous studies on the acute effect of passive smoking were performed in adult asthmatics. These studies showed conflicting results. Shephard and coworkers[28] investigated 14 asthmatic subjects during a 2 hour cigarette smoke exposure (24 ppm CO) and observed no significant changes in pulmonary function. Dahms et al.[29] reported on ten asthmatics, passively exposed to cigarette smoke (15–20 ppm CO) for 1 hour. The authors found a 21.4% decrease in FEV_1 following smoke exposure in asthmatics compared to normal controls. Knight and Breslin[30] studied six patients with asthma who developed an 11% decline in FEV_1 and an increase in bronchial reactivity to inhaled histamine 4 hours after a 1 hour smoke exposure (15–25 ppm CO). Wiedemann and coworkers[31] examined the acute effect of a 1 hour chamber exposure to cigarette smoke (40–50 ppm CO) on lung function and airway responsiveness in nine adult asthmatics, in whom no change in lung function, but a small decrease in nonspecific airway reactivity was observed. Recently, Stankus et al.[32] investigated the effect of a 2 hour exposure to tobacco smoke (8.7–14.1 ppm CO) in 21 patients with asthma who reported respiratory symptoms on previous exposure to cigarette smoke. In 7 of these 21 sub-

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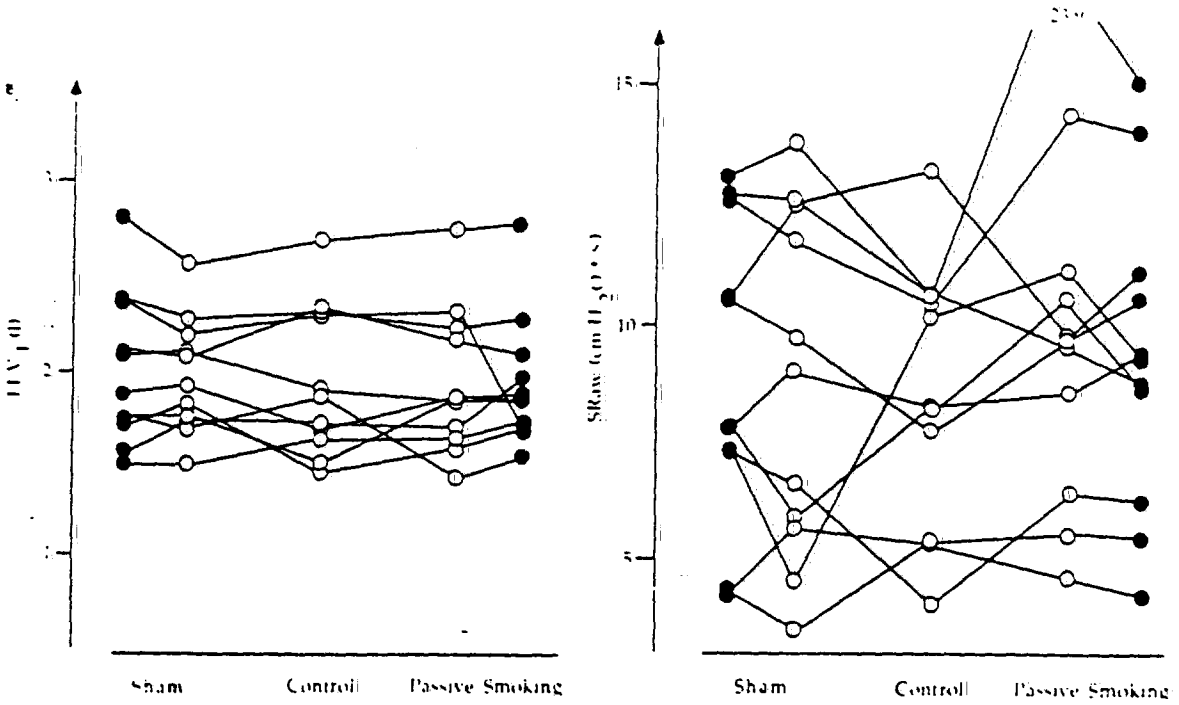

Fig. 2. FEV_1 (left) and SRaw (right) before and after exposure (Sham, passive smoking) and at the control day.

TABLE 4—Histamine Concentration (mg/mL) Necessary To Increase SRaw by 100% ($PC_{100}SRaw$) or To Decrease FEV_1 by 20% ($PC_{20}FEV_1$) After 1 Hour Exposure to Ambient Air (Sham) or Passive Smoking and at the Control Day

	Control		Sham		Passive smoking	
Patient	$PC_{100}SRaw$	$PC_{20}FEV_1$	$PC_{100}SRaw$	$PC_{20}FEV_1$	$PC_{100}SRaw$	$PC_{20}FEV_1$
1	0.25	0.09	0.51	0.27	0.30	0.21
2	0.92	0.34	5.81	0.78	6.40	1.10
3	1.60	0.73	0.38	0.11	1.24	1.05
4	1.12	1.25	2.38	0.79	1.17	0.87
5	1.45	1.72	4.59	1.68	3.16	2.64
6	2.12	1.02	3.83	1.71	6.90	3.03
7	1.07	1.13	0.59	0.60	1.45	1.57
8	0.12	0.12	0.62	0.67	1.01	1.14
9	1.85	1.28	4.80	4.22	1.40	0.75
10	0.81	0.46	0.37	0.33	0.70	0.27
11	0.66	0.30	1.24	0.68	2.79	1.00
Mean[a]	0.85	0.54	1.39	0.70	1.65	0.96
SD	2.40	2.70	3.00	2.70	2.50	2.30

[a]Geometric mean values and geometric standard deviations of mean.

jects, they found a significant (> 20%) fall in FEV_1. These findings in adult asthmatics demonstrate that there might be a subgroup of "smoke sensitive asthmatics" who develop acute airway obstruction without consistent changes in airway responsiveness following passive smoke exposure.

In our group of asthmatic children, after exposure to Sham, changes in FEV_1 between −10 and +9% were observed as compared to pre-exposure values. After passive exposure to cigarette smoke, changes of FEV_1 were within this range in nine patients. Patient no. 3 had a 13% increase in FEV_1 after smoke exposure, in contrast to a decrease of 10% after Sham. SRaw remained nearly constant both after Sham and after smoke exposure in this patient (Table 3). Patient no. 7 showed a 25% decrease in FEV_1 after smoke exposure as compared to an increase of 5% after Sham. However, there was no corresponding increase in SRaw after smoke exposure in

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this patient (Table 3). Analysis of the spirometric curves did not reveal any sign of deficient cooperation in either subject. According to our study protocol, baseline lung function measurement was performed three times on three different study days. Mean coefficients of variation were 6% for FEV_1 and 21% for SRaw, which is well within the reproducibility reported in adult subjects.[33] Therefore, we do not believe that our inability to demonstrate an adverse acute effect of passive cigarette smoking on lung function was due to an insufficient reproducibility of lung function data.

Airway hyperresponsiveness to inhaled histamine in terms of $PC_{20}FEV_1$ and $PC_{100}SRaw$ was assessed three times on three different study days. The two challenges without previous smoke exposure (control, Sham) showed a variability of ± one doubling concentration of histamine, which is within accepted limits.[33,34] Therefore, it is unlikely that our findings were due to a poor reproducibility of bronchial responsiveness measurement.

Nine of 11 asthmatic children were under regular therapy with inhaled β_2-agonists and disodium cromoglycate (and in patient no. 6 with 400 µg beclomethasone diproprionate). The duration of the effect of inhaled β_2-agonists on airway tone and bronchial responsiveness lies within 3–5 hours.[35] Therefore, as we started exposure at least 6 hours after the last inhalation therapy, an influence of β_2-agonists on our data seems to be unlikely. This may, however, not be true for disodium cromoglycate (DSCG). There are conflicting data on the protective effect of DSCG on airway responsiveness. Most authors agree that a significant protection against airway obstruction induced by histamine or methacholine cannot be substantiated.[36] Recently it has been shown that long-term treatment with DSCG may modify the level of bronchial hyperresponsiveness.[37]

In our study all children showed bronchial hyperresponsiveness to inhaled histamine, irrespective of the foregoing therapy with DSCG. Three of the 9 children with DSCG showed an increase in airway responsiveness after passive cigarette smoking, and the remaining children had decreased airway responsiveness. In comparison, one child without therapy showed an increase, and the other one without therapy a decrease in hyperresponsiveness after smoke exposure. Therefore, our inability to demonstrate an effect of passive smoke exposure on airway responsiveness in hyperresponsive children is unlikely to be explained by the concomitant treatment in these patients. Nevertheless, it seems to us that in children further investigations on the possible interaction between DSCG and passive smoking are necessary.

In the present study the level of cigarette smoke exposure was characterized by several components that per se may be potential irritants. It has been suggested that substances like CO,[38] NO_2,[39] formaldehyde,[40] and aerosolized nicotine[41] may produce upper respiratory symptoms. The threshold concentration of NO_2, which causes an increase in hyperresponsiveness during resting ventilation, is about 0.25 ppm.[39] In our experiment, total NO_x concentration was about 1 ppm; however, the reactive component, NO_2 was measured to be less than 3% of the total concentration of NO_x. Acrolein (an unsaturated aldehyde) has been demonstrated to decrease pulmonary function in guinea pigs and to produce transient bronchial hyperresponsiveness, if concentrations are at least 0.31 ppm.[42,43] In our study the concentration of acrolein was in the range of 0.1 ppm. In asthmatics, exposure to saturated aldehydes like formaldehyde in concentrations up to 3 ppm for 1–1.5 hour does not cause statistically significant decrements in pulmonary function.[40,44] In our experiment, formaldehyde concentration was about 0.13 ppm. Therefore, under our conditions concentrations of the cigarette smoke components were always lower than those effective in the single component exposure studies. Because we did not see an effect of passive smoking on lung function or airway responsiveness, synergistic effects between the constituents of cigarette smoke seem to be unlikely.

By measuring urinary cotinine concentration as an accepted biological marker of chronic exposure to passive smoking,[45–48] we found elevated levels of cotinine (> 0.5 ng/mg; Table 2) in five of six children with reported smoke exposure at home. In contrast, two of five children without a positive history showed increased cotinine levels. Therefore, in most cases low urinary cotinine levels are in accordance with a history of no passive smoking, whereas elevated levels correspond to a positive history less frequently.

Since the purpose of our study was to investigate the acute effects of passive smoking and since we did not find an effect and could not identify an active component of cigarette smoke in our experiments, it is difficult to compare our data with those of chronic exposure studies. Chronic exposure has been demonstrated to increase bronchial responsiveness and to impair lung function.[10,12,13,16,17,19–23] Our data, regarding short-term exposure, are by no means contradictory to these observations. In addition, chronic passive smoke exposure may induce changes in the airways that may mask airway response to acute exposure. From our data this hypothesis cannot be proven; however, it would be of interest to study the acute airway response of asthmatic children with and without chronic smoke exposure.

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